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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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Jeff Lloyd
Saliwanchik, Lloyd & Saliwanchik
2421 N.W. 41st Street Suite A-1
Gainesville,, FL 32606-6669

EXAMINER
LI, QIAN J

ART UNIT	PAPER NUMBER
2632	

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Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/593,629	CAMERON ET AL.
Examiner	**Art Unit**
Q. Janice Li	1632

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *04 March 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *25-27,29-35,38-41,43,45-50 and 52-62* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *25-27,29-35,38-41,43,45-50 and 52-62* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *13 June 2000* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The Declaration and amendment filed on March 7, 2003 have been entered as Papers #14 & 15. Claims 25, 29-35, 40, 41, 43, 49, 50, and 52 have been amended. Claims 28, 36, 37, 42, 44, and 51 are canceled. Claims 56-62 are newly submitted. Claims 25-27, 29-35, 38-41, 43, 45-50, and 52-62 are pending and under current examination.

Unless otherwise indicated, previous rejections that have been rendered moot in view of the amendment to pending claims and the Declaration will not be reiterated. The arguments in paper #15 are moot in view of new grounds of rejection.

Information Disclosure Statement

The co-pending applications disclosed in the newly submitted information disclosure statement (IDS) have been considered by the Examiner. However, they are not suitable to be included in the patent publication, therefore, have been deleted from PTO-1449.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 25-27, 35, 38-40, 43, 48, 49, 59, are newly rejected under 35 U.S.C. 102(b) as being anticipated by *Hadley et al* (J Cell Biol 1985;101:1511-22).

The amended product claims are now drawn to a biochamber comprising a Sertoli cell formed lumen containing non-Sertoli cells in the lumen structure. The Declaration indicated that such lumen structure would only form when the Sertoli cells are cultured in the presence of a basement membrane preparation for a period of time such that epithelial-like junctions are formed between adjacent Sertoli cells and the Sertoli cells form a discreet outer wall that defines a lumen. The revised method claims are drawn to co-culturing Sertoli cells and non-Sertoli cells in the presence of a BM preparation.

Hadley et al teach a method comprising co-culturing Sertoli cells and non-Sertoli cells (germ cells) in the presence of a basement membrane preparation (reconstituted basement membrane, RBM gel) for a period of time so that peripheral (basal) and central compartment (adluminal) of cords are formed. Tight junctions are observed between adjacent Sertoli cells, and germ cells are residing in the peripheral and central Sertoli cell formed compartments (See pages 1513-1517, particularly § Thick-layered RBM and figure 5b). In figure 5b, a monolayer of Sertoli cells makes up the central compartment (lumen) surrounding and containing spermatocytes. Therefore, *Hadley et al* anticipate instant claims.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 25, 29, 30, 33, 34, 40, 46, 47, 50, 52-56 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Selawry* (US 5,843,430), in view of *Hadley et al* (J Cell Biol 1985;101:1511-22).

Selawry teaches a method of co-culturing Sertoli cells with pancreatic islet cells (column 8, lines 39-43; and column 18, lines 44-46). *Selawry* teaches that transplanting pancreatic islet in conjunction with Sertoli cells created an immunologically privileged site upon transplanting the co-culture to diabetic rats (abstract and example 6). *Selawry et al* do not teach making a biochamber by co-culturing the Sertoli cells and non-Sertoli cells in the presence of a basement membrane preparation.

Hadley et al teach a method comprising co-culturing Sertoli cells and non-Sertoli cells (germ cells) in the presence of a basement membrane preparation (reconstituted basement membrane, RBM gel) for a period of time so that a central compartment (lumen) of cords and tight junctions are formed between adjacent Sertoli cells, and germ

cells are residing in the central compartment (See pages 1513-17, particularly § Thick-layered RBM and figure 5b). They go on to teach that the tight junction between Sertoli cells would form when Sertoli cells are cultured in a layer of RBM after a week, and particularly on a thick layer of RBM. They also teach that these junctions constitute a permeability barrier that excludes intercellular substance such as tracers from the central compartment of cords (left column, page 1517). *Hardley et al* do not teach co-culturing the Sertoli cells with islet cells.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Selawry et al* by simply employ the culture method taught by *Hadley et al* in the process as taught by *Selawry et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the process because the therapeutic cells surrounded by Sertoli cells having the tight junction would provide better protection for therapeutic cells, preventing or reducing a host immune response. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 25, 29-34, 40, 46, 47, 50, 52-56 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Sanberg et al* (US 5,942,437), in view of *Hadley et al* (J Cell Biol 1985;101:1511-22).

Sanberg et al teach a method of co-culturing Sertoli cells with therapeutic cells (abstract) including islet cells, neurons (column 1, line 33), adrenal chromaffin cells (column 2, lines 12-13), embryonic dopaminergic cells (column 2, line 28), and NT2

neuronal cells (column 11, lines 20-39). *Sanberg et al* go on to teach that the method provides increased viability, number, survival, and maturation of therapeutic cells for transplantation or for cryopreservation. *Sanberg et al do* not teach making a biochamber by co-culturing the Sertoli cells and non-Sertoli cells in the presence of a basement membrane preparation.

Hadley et al teach a method comprising co-culturing Sertoli cells and non-Sertoli cells (germ cells) in the presence of a basement membrane preparation (reconstituted basement membrane, RBM gel) for a period of time so that a central compartment (lumen) of cords and tight junctions are formed between adjacent Sertoli cells, and germ cells are residing in the central compartment (See pages 1513-17, particularly § Thick-layered RBM and figure 5b). They go on to teach that the tight junction between Sertoli cells would form when Sertoli cells are cultured in a layer of RBM after a week, and particularly on a thick layer of RBM. They also teach that these junctions constitute a permeability barrier that excludes intercellular substance such as tracers from the central compartment of cords (left column, page 1517). *Hardley et al* do not teach co-culturing the Sertoli cells with islet or neuronal cells.

However, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Sanberg et al* by simply employ the culture method taught by *Hadley et al* in the process as taught by *Sanberg et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the process because the therapeutic cells surrounded by Sertoli cells having the tight junction would provide better protection for therapeutic

cells, preventing or reducing a host immune response. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 45, 57, 59, and 60 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Sanberg et al* (US 5,942,437), and *Hadley et al* (J Cell Biol 1985;101:1511-22) as applied to claims 25, 29-34, 40, 46, 47, 50, and 52-56 above and further in view of *van der Wee et al* (Exp Cell Res 1999;252:175-85).

Hadley et al do not teach using a matrigel as the basement membrane preparation. *Van der Wee et al* teach using growth factor reduced matrigel to form hollow seminiferous tubules (lumen) containing a wall formed by mono- or multi-layers of Sertoli cells (See 1st section under Results, fig. 2).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Sanberg et al* and *Hadley et al* by simply substituting the RBM with the matrigel as taught by *van der Wee et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because both materials are known to be able to support the Sertoli cell forming seminiferous tubules *in vitro*. Thus, the claimed invention as a whole was *prima facie* obvious in the absence of evidence to the contrary.

Claims 41, 58, 61, and 62 are newly rejected under 35 U.S.C. 103(a) as being unpatentable over *Sanberg et al* (US 5,942,437), *Hadley et al* (J Cell Biol

1985;101:1511-22) and *van der Wee et al* (Exp Cell Res 1999;252:175-85) as applied to claims 25, 29-34, 40, 45-47, 50, 52-57, 59, 60 above and further in view of *Spaulding* (US 6,001,643).

The combined teachings of *Sanberg et al*, *Hadley et al*, and *van der Wee et al* fail to suggest co-culture Sertoli cells and therapeutic cells with a microgravity method.

Spaulding teaches that microgravity culture is known in the art as one of many culture methods which generate a quiescent microgravity like environment, particularly suitable for three dimensional culture (column 3, lines 17-35).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the methods taught by *Sanberg et al*, *Hadley et al*, and *van der Wee et al* by simply substituting the routine culture method with the microgravity culture as taught by *Spaulding et al* with a reasonable expectation of success. The ordinary skilled artisan would have been motivated to modify the claimed invention because the later could better preserve the three-dimensional structure formed by the Sertoli cells. Thus, the claimed invention as a whole was clearly *prima facie* obvious in the absence of evidence to the contrary.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Q. Janice Li whose telephone number is 703-308-7942. The examiner can normally be reached on 8:30 am - 5 p.m., Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Deborah J. Reynolds can be reached on 703-305-4051. The fax numbers for the organization where this application or proceeding is assigned are 703-872-9306 for regular communications and 703-872-9307 for After Final communications.

Any inquiry of formal matters can be directed to the patent analyst, Dianiece Jacobs, whose telephone number is (703) 305-3388.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-1235. The faxing of such papers must conform to the notice published in the Official Gazette 1096 OG 30 (November 15, 1989).

Q. Janice Li
Examiner
Art Unit 1632

QJL
May 23, 2003

ANNE M. WEHBE' PH.D
PRIMARY EXAMINER